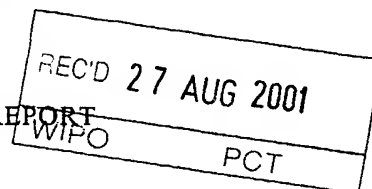


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



3

Applicant's or agent's file reference GM50049	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/12103	International filing date (day/month/year) 04 MAY 2000	Priority date (day/month/year) 10 MAY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/68; C12P 19/34 and US Cl.: 435/6, 91.2		
Applicant SMITHKLINE BEECHAM CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets.
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
 These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 08 NOVEMBER 2000	Date of completion of this report 23 FEBRUARY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer JEHANNE SOUAYA TERRY J. DEY PARALEGAL SPECIALIST TECHNOLOGY CENTER 1600
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

I. Basis of the report1. With regard to the **elements** of the international application:*☒ the international application as originally filed☒ the description:pages 1-22 , as originally filedpages NONE , filed with the demandpages NONE , filed with the letter of _____☒ the claims:pages 23-30 , as originally filedpages NONE , as amended (together with any statement) under Article 19pages NONE , filed with the demandpages NONE , filed with the letter of _____☒ the drawings:pages none , as originally filedpages NONE , filed with the demandpages NONE , filed with the letter of _____☒ the sequence listing part of the description:pages NONE , as originally filedpages NONE , filed with the demandpages NONE , filed with the letter of _____2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages none☒ the claims, Nos. none☒ the drawings, sheets/fig none5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/12103

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims <u>1-32</u>	YES
	Claims <u>none</u>	NO
Inventive Step (IS)	Claims <u>1-32</u>	YES
	Claims <u>none</u>	NO
Industrial Applicability (IA)	Claims <u>1-32</u>	YES
	Claims <u>none</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1-32 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method for inserting a cassette into a nucleic acid molecule without requiring ligation.

----- NEW CITATIONS -----

NONE

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12Q 1/68, C12P 19/34	A1	(11) International Publication Number: WO 00/68428 (43) International Publication Date: 16 November 2000 (16.11.00)
(21) International Application Number: PCT/US00/12103 (22) International Filing Date: 4 May 2000 (04.05.00) (30) Priority Data: 60/133,391 10 May 1999 (10.05.99) US (71) Applicants (for all designated States except US): SMITHK- LINE BEECHAM CORPORATION [US/US]; One Franklin Plaza, Philadelphia, PA 19103 (US). SMITHK- LINE BEECHAM PLC [GB/GB]; New Horizons Court, Great West Road, Brentford, Middlesex TW8 9EP (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): CHALKER, Alison, F. [GB/US]; 137 Harvard Drive, College Woods, Trappe, PA 19426 (US). GE, James, Yigong [CN/US]; 50 Keokuk Road, Royersford, PA 19468 (US). HOLMES, David, J. [GB/US]; 126 Woodmint Drive, West Chester, PA 19380 (US). LUNSFORD, Robert, D. [US/US]; 2026 Deer Ridge Drive, Pottstown, PA 19380 (US). (74) Agents: GIMMI, Edward, R. et al.; SmithKline Beecham Corporation, Corporate Intellectual Property, UW2220, 709 Swedeland Road, P.O. Box 1539, King of Prussia, PA 19406-0939 (US).		(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>
(54) Title: METHODS FOR PRODUCING MODIFIED NUCLEIC ACID MOLECULES		
(57) Abstract A method for inserting a cassette into a nucleic acid molecule to produce a modified nucleic acid molecule, e.g., a nucleic acid-cassette fusion, is described. The method involves the use of polymerase chain reaction, thereby permitting precise targeting of the desired site in the molecule, but does not require ligation. Also described is the use of this method for high throughput screening the resulting modified nucleic acid molecules.		

FOR THE PURPOSES OF INFORMATION ONLY

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DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/12103

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C12P 19/34

US CL : 435/6, 91.2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	NIKAWA et al. PCR- and Ligation- Mediated Synthesis of Marker Cassettes with Long Flanking Homology Regions for Gene Disruption in <i>Saccharomyces Cerevisiae</i> . Nucleic Acids Research. 1998, Vol. 26, No. 3, pages 860-861.	1-32

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

13 AUGUST 2000

Date of mailing of the international search report

30 AUG 2000

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JEHANNE SOUAYA

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/12103

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

STN, Medline, Caplus, Uspatful, EAST

nucleic acid, cassette, no ligation, pcr, insertion, construction, nucleic acid cassette fusion

SEQUENCE LISTING

<110> SMITHKLINE BEECHAM CORPORATION
SMITHKLINE BEECHAM plc

<120> METHOD FOR PRODUCING MODIFIED NUCLEIC
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<130> GM50049

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